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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/978,297	10/17/2001	Oron Yacoby-Zeevi	01/22716	5033

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G.E. EHRLICH (1995) LTD.
c/o ANTHONY CASTORINA
SUITE 207
2001 JEFFERSON DAVIS HIGHWAY
ARLINGTON, VA 22202

EXAMINER

HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 10/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/978,297

Applicant(s)

YACOBY-ZEEVI, ORON

Examiner

Richard G. Hutson

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,7-9,11-17 and 19-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7-9,11-17 and 19-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/5/2005 has been entered.

Applicants amendment of the drawings, specification and claims 1, 7, 13, 21, 26 and 31, and the cancellation of claims 38-50, in the paper of 7/13/2005 is acknowledged. Claims 1-5, 7-9, 11-17 and 19-37 are present for examination. Applicants' arguments filed on 4/5/2005, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Specification

The disclosure is objected to because of the following informalities:

Applicants newly added figure 2, contains sequences that should be identified by a sequence identifier either in the figure or the description of the figure.

2422.02 The Requirement for Exclusive Conformance; Sequences Presented in Drawing Figures

...It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ("SEQ ID NO:X") must be used, either in the drawing or in the Brief Description of the Drawings.

Appropriate correction is required.

Claim Objections

Claims 1-5, 7-9, 11-17 and 19-37 are objected to because of the following informalities: Claims 1, 7, 13, 21, 26 and 31 each recite "an mature form". It is suggested that this be amended to "a mature form".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 7-9, 11-17 and 19-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5, 7-9, 11-17 and 19-37 are indefinite in that they are unclear in the recitation "mature form" in reference to the heparanases of a) and b). It is unclear what applicants intend to be encompassed by the "mature form" of the referred to heparanases.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1652

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-5, 7-9, 11, 12, 13-17, 19, 20, 21-25, 26-30 and 31-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fuks et al., Gough et al., (U.S. Patent No: 5,962,321) and Goshen et al. (Molecular Human Reproduction, Vol 2, No. 9, pp 679-684, 1996, see IDS).

Fuks et al. teach that the plasma membrane, extracellular matrix and basement membranes of all tissue types contain among other constituents, complex macromolecules referred to as heparan sulfate proteoglycans (HSPG). Fuks et al. teach that heparan sulfate proteoglycans have an intimate interrelationship with other macromolecules which make up the extracellular matrix, and thus their degradation may have a profound effect on the regulation of cell anchorage, movement, function and growth. Fuks et al. further teach that a number of normal physiological conditions are associated with the degradation of the extracellular matrix of various tissues, such as neutrophil mobilization in which the cells must penetrate the endothelium of blood vessels and the underlying basal lamina in order to reach the target tissue. Fuks et al. teach the purification of heparanase obtained from human SK-HEP-1 cells, and its use in formulations for therapies in which the release of FGF from the extracellular matrix would be a desirable effect such as those situations in which angiogenesis and/or the growth of fibroblasts is desired such as wound healing, ovulation, and transplantation. It

Art Unit: 1652

is recognized that the heparanase taught by Fuks et al. inherently has the amino acid sequence of SEQ ID NO: 1.

Goshen et al. teach that the cleavage of heparin sulphate results in the disassembly of the extracellular matrix and a key role in cell invasion associated with metastasis, inflammation and placentation. Goshen et al. further teach the purification and characterization of placental heparanase and its expression by cultured cytotrophoblasts. Goshen et al. teach that the placental heparanase resembles heparanase expressed by highly metastatic tumour cells and activated cells of the immune system. Goshen et al. further propose that cytotrophoblast heparanase facilitates placentation, through cytotrophoblast extravasation and localized neovascularization.

Gough et al. teach methods for improving embryo implantation by treating embryos with leukemia inhibitory factor (LIF). Gough et al. teach that a major difficulty associated with in vitro fertilization (IVF) and embryo transfer (ET) programs particularly in humans is the low success rate achieved on implantation of fertilized embryos and thus treatment of embryos with LIF increases the percentage of embryos that are successfully implanted.

One of ordinary skill in the art at the time of filing would have been motivated to practice the methods of Gough et al. for increasing the implantation of embryos by additionally adding heparanase as taught by Fuks et al. to either an embryo (IVF and trophoblast cells), a receptive uterus, or both prior to implantation of the embryo in the receptive uterus as a means of degrading the extracellular matrix associated with the

Art Unit: 1652

uterus, and thus improving embryo implantation in the uterus. This motivation comes from the teachings of Goshen et al. who teach that the embryo cytotrophoblast express a heparanase which resembles that of malignant cells, and the importance of this enzyme in cell invasion associated with placentation. The reasonable expectation of success comes from the results of Gough et al. who teach similar methods of treatment of embryos with LIF as well as the teaching of Goshen et al. who teach the importance of heparanase in cytotrophoblast invasion associated with placentation. Thus claims 1-5, 7-9, 11, 12, 13-17, 19, 20, 21-25, 26-30 and 31-37 are made obvious by Fuks (U.S. Patent No. 5,362,641), Gough et al., (U.S. Patent No: 5,962,321) and Goshen et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1652

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Richard G. Hutson', with a large, sweeping flourish extending to the right.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rg
9/21/2005